REMARKS

Claims 2-26 and 28-31 are pending herein. By this Amendment, Claims 1 and 27 are canceled without prejudice or disclaimer, and Claims 2, 4, 6, 8-24, and 30 are amended. No new matter is added by this Amendment.

Applicants thank Examiner Oh for indicating that Claims 28-31 are allowed. Applicants also thank Examiner Oh and Primary Examiner Kishore for the courtesies extended to their representative during a March 6, 2003 telephonic interview and an October 15, 2003 personal interview. Applicants also thank Examiner Oh for indicating that the dependent claims may be amended to depend from the allowed claims and that Claim 30 may be amended to delete the word "sprayed" during a October 27, 2003 telephonic interview. Applicants' separate record of the interviews is set forth in the foregoing amendments and the following remarks.

Entry of the Amendment is proper because it: (a) places the application in condition for allowance; (b) does not raise any new issues requiring further search and/or consideration; and (c) does not present any additional claims without canceling a corresponding number of finally rejected claims.

I. REJECTION UNDER 35 U.S.C. 103(a)

Claims 1-7 were rejected under 35 U.S.C. 103(a) over U.S. Patent No. 5,681,583 (Savastano et al.) in view of U.S. Patent No. 5,455,268 (Watanabe et al.) and U.S. Patent No. 5,574,062 (Hashimoto et al.). Applicants' representative called Examiner Oh on March 6, 2003 to request clarification as to Claims 8-27, which were indicated as allowable. During the March 6, 2003 telephone conference, the Examiner indicated that

Claims 8-27 were also rejected even though the Office Action states explicitly to the contrary. This rejection is respectfully traversed.

Savastano discloses a drug delivery device having two embodiments. The first embodiment of the drug delivery device is for delivery of an active agent to a pre-selected region of the gastrointestinal tract, particularly the colon (col. 1, lines 10-13; col. 3, lines 25-30). The colonic delivery device comprises: (1) a solid core comprising an active agent; (2) a delay jacket coated over the core; (3) a semi-permeable membrane coated over the delay jacket; and (4) optionally an enteric coating over the semi-permeable membrane (col. 5, lines 30-45). The colonic drug delivery device resists dissolution in gastric acid for at least two hours, thereby allowing delivery of the active agent to the colon (col. 5, line 61 - col. 6, line 14). See also Example 2: Dissolution Test. The second embodiment of the drug delivery device is for delivery of an active agent intermittently at pre-selected times. For delivery of an active agent intermittently, the drug delivery device includes an additional layer of active agent between the delay jacket and the semi-permeable membrane (col. 12, lines 15-21). See Example 4. Savastano discloses that the active agent may be a 5-lipoxygenase inhibitor (col. 6, lines 33-35). However, as acknowledged by the Examiner, Savastano does not disclose esculetin or any derivative thereof.

Watanabe does not overcome the deficiencies of Savastano. Watanabe discloses esculetin derivatives as agents for protecting cartilage, for example, in patients with rheumatoid arthritis or osteoarthritis (col. 1, lines 8-53). Watanabe does not teach or suggest substituting esculetin or its derivatives, which are used for protecting cartilage, in the drug delivery device of Savastano for treating diseased colonic tissue. Watanabe also does not teach or suggest substituting esculetin in the delivery device of Savastano for

drugs to be delivered **intermittently** at pre-selected times. Such a combination is based upon impermissible hindsight reconstruction using the claimed invention as a template and without regard to the teachings of Savastano and Watanabe.

Furthermore, with regard to Claims 9 and 11-17 as discussed at the interview, an objective of the claimed controlled-release preparation is to **maintain** the concentration of glucuronic acid conjugates in plasma at 0.5 μmol/L or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg. Neither of the references teach or suggest a controlled release system which maintains a concentration of glucuronic acid conjugates as claimed. Even if the references were properly combinable, which they are not, Applicants' claimed invention would not be obtained. Thus, it would not have been obvious for one of ordinary skill in the art to make the claimed preparations in view of the combined teachings of Savastano and Watanabe.

Hashimoto does not overcome the deficiencies of Savastano and Watanabe. Hashimoto discloses coumarin derivatives inhibiting 12-lipoxygenase as medicines for preventing circulatory diseases and preventing the metastasis of some kinds of cancers (col. 1, lines 9-20). Hashimoto also discloses that esculetin is known to inhibit 5-lipoxygenase and 12-lipoxygenase of mastocytoma cells (col. 2, lines 49-64). Like Watanabe, Hashimoto does not teach or suggest substituting esculetin or its derivatives in the colonic drug delivery device of Savastano for treating diseased colonic tissue. Hashimoto also does not teach or suggest substituting esculetin in the delivery device of Savastano for drugs to be delivered intermittently at pre-selected times. As noted, an objective of the claimed controlled-release preparation is not to stop and start drug administration at different times, but to maintain the concentration of glucuronic acid

conjugates in plasma at 0.5 μmol/L or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

Thus, it would not have been obvious for one of ordinary skill in the art to make the claimed preparations in view of the combined teachings of Savastano, Watanabe, and Hashimoto. Nevertheless to advance prosecution, Claims 1 and 27 are canceled, and Claims 2, 4, 6, and 8-10 are amended to depend directly or indirectly from allowed Claim 28 or Claim 30, thereby rendering the rejection moot. Further, Claim 30 is amended as requested by Primary Examiner Kishore at the examiner interview to recite the transition "consisting essentially of". Reconsideration and withdrawal of the rejection are respectfully requested.

II. CONCLUSION

In light of the foregoing remarks, this application is in condition for allowance, and early passage of this case to issue is respectfully requested. If there are any questions regarding this Amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application.

If there are any discrepancies in the fees, please charge or credit our Deposit Account No. 501032 (Docket No. FJIN-109).

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence dated 10/28/03 is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on 10/28/03.

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